

Att'y Dkt. No. US-1460

U.S. App. No: 10/023,711

REMARKS

Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the following remarks. The claims have been amended to further clarify the invention. As this amendment does not introduce new issues, but seeks to clarify the claims, applicants earnestly solicit entry thereof.

The Rejection of Claims 1-6 under 35 U.S.C. §112, 1st Paragraph

The Examiner asserts that claims 1-6 contain subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. The Examiner has asserted that the claims are directed toward "any method of making an L-amino acid by culturing an *Escherichia coli* bacterium having any mutation to any gene of any nucleotide sequence and structure encoding any RMF protein of any amino acid sequence and structure." Applicants specifically amended the claims to recite that the *rmf* gene is located on the chromosome of *Escherichia coli*, however, the Examiner has completely ignored this limitation in his assessment of the claim scope. Applicants respectfully disagree with the Examiner's assessment, and submit that the claims are limited to the *rmf* gene of *E. coli*.

Applicants respectfully submit, therefore, that the claims are fully and adequately described in the specification. The claims encompass a specific method for producing an L-amino acid via bacterial cell culture (all very well-known methods) whereby the gene encoding the *E. coli* RMF protein (a known gene and protein sequence) or an expression control sequence thereof (also known) is mutated so that the RMF protein is inactive. See page 13, line 20 to page 17, line 4. The inactivation of the RMF protein by

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disrupting the RMF gene, or a sequence which controls its expression, is the point of novelty. Applicants have discovered that when this known gene is disrupted so that the resulting protein is inactive, L-amino acid production is increased as compared to a bacterial cell having an active RMF protein.

The claim is a genus claim, as the Examiner has pointed out, however, but this does not mean that it automatically is not described if only a few species are specifically exemplified. Applicants are not required to describe every species within the genus. The Examiner must also evaluate if there is a common technical feature among the species of the genus which would allow one of ordinary skill in the art to determine that applicants were in possession of the invention as described. The common technical feature of the claimed invention is that disruption of the *E. coli* *rmf* gene results in increased production of amino acids by the bacterial cell transformed with the disrupted *rmf* gene. Claim 1 clearly possesses this common technical feature of the disruption of the known *E. coli* RMF gene. Obviously, disruption of the gene can occur many ways and will result in many variations of the gene. The Examiner is correct in determining that the genus is highly variable, however, again this does not mean the invention is not adequately described. One of ordinary skill in the art would know what actions are necessary to disrupt the gene so that the protein is inactive, since the threshold of expectation of success is very low. Disruption of the gene and determining other species whereby the gene will express an inactive protein is much easier to do and predict, and within routine experimentation than, for example, determining variants so that the gene will express an active form of the protein.

Furthermore, Applicants were the first to disclose that the production of L-lysine

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can be improved by disrupting the *rmf* gene. While the *rmf* gene is expressed during the stationary phase of the culture and the protein translation activity is decreased in the wild-type strain, Applicants surprisingly found that the decrease of protein translation activity is prevented or reduced in a strain in which the normal RMF protein does not function normally (see page 17, lines 15-22). Therefore, clearly the present specification describes that production of an L-amino acid other than L-lysine is also improved in a strain in which the RMF protein does not function normally.

The invention is adequately described, therefore, since all the species do not have to be explicitly set forth in order to sufficiently describe the genus, as long as a common technical feature is present which can be readily ascertained. Limiting the claimed invention to the working examples is not the requirement of the written description, as the Examiner has implied. Applicants must sufficiently describe their invention to ensure the person of skill in the art that they were in possession of their invention. Clearly, applicants have adequately described the invention of disruption of the *rmf* gene and the resulting increase in amino acid production and excretion by the *Escherchia coli* cell. This common technical feature binds together all of the species of the claimed genus, and hence the invention is adequately described.

Applicants respectfully request that the rejection be withdrawn in light of the above comments.

Claims 1-6 are also rejected under 35 U.S.C. §112, 1st paragraph for non-enablement. The Examiner asserts that the SEQ ID No. of the inactivated *rmf* gene is critical or essential to the practice of the invention, but is not included in the claims.

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Applicants respectfully disagree and set forth the following arguments. The Examiner has stated that the specification provides guidance for transformed *E. coli* host cell containing an inactivated *E. coli* *rmf* gene which is used in the recombinant production of acid phosphatase and L-lysine. This is exactly what is claimed. Again, it is not evident that the Examiner has recognized that the claims have been limited to the *rmf* gene of *E. coli*. The Examiner then states that the specification does not provide the SEQ ID No. of the *rmf* gene. It is unclear why the Examiner is requiring a SEQ ID No. (or a sequence listing) for a known gene/protein, as this is not required under 37 C.F.R. §§1.821 to 1.825.

There is no requirement to provide a sequence listing for sequences which are known in the prior art. See 37 C.F.R. 1.821(c). It is not necessary to provide information in the specification which is well-known in the prior art, in fact it is preferable to omit such information. See *Spectra Physics, Inc. v. Coherent Inc.*, 827 F.2d 1524 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 954 (1987). The crux of the invention is not the discovery of a new gene or protein sequence, which would require submission of a sequence listing under the rules, but that the disruption of a known gene sequence in an *E. coli* bacterium results in increased production of L-amino acids by the bacterium. The *rmf* gene from *E. coli* is known in the prior art, as cited in the specification (see page 1, line 20). Therefore, there is no requirement to recite this sequence as part of a sequence listing.

The Examiner has suggested that the claims encompass *rmf* genes from different biological sources, however, the claims encompass the *rmf* gene from *E. coli*, which the Examiner has failed to acknowledge. The claims previously presented after first action

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were limited to the *rmf* gene from *E. coli*, however, the claims have been amended to further clarify this fact. If the Examiner still believes that the claims are directed to the *rmf* gene from different biological sources, then applicants respectfully request that the Examiner further explain and clarify his position.

In light of the foregoing arguments, one of ordinary skill in the art would be enabled to practice the steps of the claimed method, and therefore, applicants respectfully submit that the claims are fully enabled and request that the rejection be withdrawn.

The Rejection of Claims 1-6 under 35 U.S.C. §112, 2nd Paragraph

The Examiner has rejected claims 1-6 under 35 U.S.C. §112, 2nd paragraph, asserting that the phrase "controlling sequence of *rmf* gene" is vague and indefinite. Applicants have amended the claims to remove this language, and insert the phrase "expression control sequence" which is clearly defined on page 13 of the specification. Applicants respectfully submit that the claims as amended are definite and request that the rejection be withdrawn.

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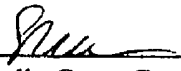
Conclusion

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Fronda believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, he is invited to call on the number below.

It is not believed that extensions of time are required beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the undersigned respectfully requests that she be contacted immediately.

Respectfully submitted,

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